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Estimation of Basic Reproduction Number R_0 for SEIR Dengue Fever Model

The Case of Dengue in Pakistan

Hassan Shah
Student of MS Mathematics,
U.E.T Peshawar, Pakistan

Muhammad Javid
Student of MS Mathematics,
U.E.T Peshawar, Pakistan

Noor Badshah
Department of Basic Sciences,
U.E.T Peshawar, Pakistan

Muhammad Adil
Regular student of MS Mathematics,
U.E.T Peshawar, Pakistan

Abstract— **In this paper, we mainly focus on the transmission of dengue fever with the aim of analyzing and comparing logistic and exponential curve that occurred in Lahore (Pakistan), in the year 2010–-2011. We obtain the force of infection, ∧, from the real data of Lahore, and then computed the basic reproduction number, R_0. Based on the analysis of the behaviour of R_0, we show that the disease is epidemic in the region. We also compare the values of logistic fit and exponential approximation to find their relative percent error.**

Keywords—SEIR Model; Endemic; Epidemic; Reproduction number; Force of infection.

I. INTRODUCTION

Dengue fever, a mosquito-borne viral infection found in tropical and subtropical regions worldwide. The World Health Organization estimates that today more than 2.5 billion people are at high risk for Dengue fever [18]. Currently the disease is endemic in more than 100 countries, and is spreading throughout the world. Dengue disease is caused by four antigenic-ally related but distinct serotypes namely DEN-1, DEN-2, DEN-3 and DEN-4 in which only DEN-2 and DEN-3 are mostly found in tropical countries [5]. It is transmitted to the human body by biting an infected female Aedes Aegypti or Aedes Albopictus mosquitoes as the primary mosquito vector. Infection by any single type apparently produces permanent immunity to that particular serotype to which the patient is exposed, but only temporary cross immunity to the other three serotypes (Cunha, 2007; WHO, 2002). Infection with one of these viruses i.e., DEN-1, DEN-2, DEN-3 or DEN-4, characteristically results in fever, headache and rash. The clinical spectrum can vary, however, from asymptomatic to more severe infections with bleeding and shock. A second infection by this virus can result in a more virulent form of the disease known as dengue hemorrhagic fever (DHF).

In twentieth century the disease was common in Asia and Pacific [17]. In Asia, the first confirmed outbreak of DHF occurred in Philippines and Thailand in the year 1950. However, in the mid of the year 1970, the disease spread throughout South East Asia. Thereafter in the next 20 years, dengue transmission is epidemic every 3–5 years in hyper endemic areas [15].

In Pakistan, the first confirmed dengue haemorrhagic fever outbreak was due to serotype DEN-2 reported in June 1994 by Aga Khan University Hospital (AKUH) [4]. Thereafter, a large number of DHF cases have been reported from different parts of the country. Akram et al. reported that two serotypes namely DEN-1 and DEN-2 were founded in the sera of children with undifferentiated fever [1]. In 1998, an outbreak of dengue fever in the Baluchistan province was occurred due to co-circulation of DEN-1 and DEN-2 [14]. In year 2005, a number of DHF cases due to serotype DEN-3 were reported in different hospitals of Karachi [8]. Thereafter, in year 2006, about 3,640 cases of DHF due to serotypes (DEN-2 and DEN-3) were admitted to several hospitals in the country [11].

The dengue disease transmission cycle starts with a dengue infected host body. The virus circulating in the blood of these infected bodies in the viremic period (4 to 7 days) called intrinsic incubation period [6, 8]. During this viremic period, an uninfected female Aedes aegypti mosquito bites a human body and ingests blood that contains dengue virus. Then an extrinsic incubation period begins within the mosquito (vector). Extrinsic incubation period is about 8 to 12 days. After that the salivary glands of the mosquito become infected and the virus is transmitted when the infected mosquito bites and injects the salivary fluid into the wound of the human body.

The life span of Aedes aegypti mosquito is about fourteen days. Infected female mosquitoes never recover from the infection since their infective period ends with their death [6]. As no vaccine presently exists, the only method of controlling or preventing dengue and DHF is to combat or eradicate the mosquito vectors [18]. Relative humidity and temperature of the region affects the development of the mosquitoes as well as

dengue viral development. As we see in Pakistan, dengue cases are generally at peak in June, July and August. To control the dengue and dengue hemorrhagic fever effectively, we should understand the dynamics of the disease transmission and take into account all of the relevant details.

In this paper, we used a dengue fever transmission model that was earlier proposed by Pinho et al. in 2010. The human population is divided into susceptible, exposed, infected and recovered classes, while the vector population is divided into aquatic, susceptible, exposed and infected classes. The proposed model is tested on real epidemic data of Lahore (Pakistan). The model shows that there is a reproductive ratio R_0 that conceptualizes the rate of spread of a dengue disease and determines a threshold: whenever $R_0 < 1$, a typical infective give rise, on average, to less than one secondary infection, and the disease will die out. Otherwise when $R_0 > 1$, the disease will persist in the population [10].

II. A MATHEMATICAL MODEL FOR DENGUE FEVER IN A VIRGIN ENVIRONMENT

In this paper, we use a Dengue fever model proposed by Pinho et al. in 2010 [16]. In this model, host population $N_H(t)$ is divided into four compartments, one is known as susceptible (a class of human which is exposed to be infected), denoted by $S_H(t)$, second one is exposed class which is denoted by $E_H(t)$, third is infected class which is denoted by $I_H(t)$, and forth a recovered class (those individuals which are from diseases or removed), denoted by $R_H(t)$. Vector (mosquitoes) population $N_V(t)$ is divided into four compartments, one is called aquatic class, denoted by $A_V(t)$, second one is a class that potentially infected by dengue virus $S_V(t)$, third class is exposed class denoted by $E_V(t)$ and mosquitoes that were infected with dengue virus $I_V(t)$.

The Pinho model is a system of eight ordinary differential equations. The block diagram of the model is given in Figure (1). Using Block diagram in Figure (1), the dynamical system for host (human) and vector (mosquitoes) population are described by the following two systems of ordinary differential equations:

$$\left.\begin{aligned}
\frac{dS_H(t)}{dt} &= \lambda N_H(t) - \alpha\beta_m S_H(t) I_V(t)/N_H(t) - \lambda S_H(t)\\
\frac{dE_H(t)}{d(t)} &= \alpha\beta_m S_H(t) I_V(t)/N_H(t) - (\theta_i + \lambda) E_H(t)\\
\frac{dI_H(t)}{dt} &= \theta_i E_H(t) - (\gamma + \lambda) I_H(t)\\
\frac{dR_H(t)}{dt} &= \gamma I_H(t) - \lambda R_H(t)
\end{aligned}\right\} \quad (1)$$

where λ is the birth and death rates of human population, μ is the mortality rate of vector population, α is the mean number of bites per day per vector per host, βm is the effective contact rate, ca and cm are the control effort rates, C is the vector carrying capacity, γ is the inverse of the duration of host viraemia, μ is the mortality rate of the vectors, μa is the average aquatic mortality rate, γm is the mean aquatic transition rate, k is the hatched from all eggs, δ is the mean oviposition rate, θe (extrinsic) and θi (intrinsic) incubation rates of vector and host populations respectively.

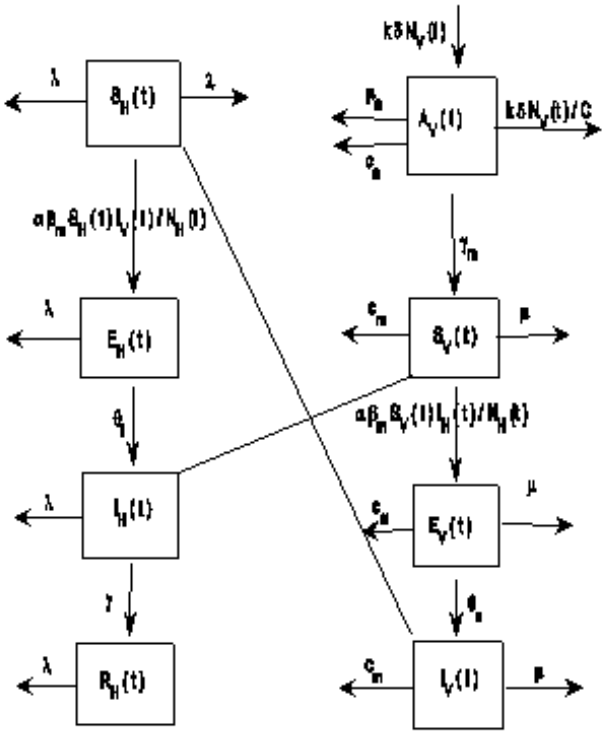

Figure 1. Block Diagram of SEIR Dengue Fever Model

$$\left.\begin{aligned}
\frac{dA_V(t)}{dt} &= k\delta(1 - A_V(t)/C) N_V(t) - (\gamma_m + \mu_a + c_a) A_V(t)\\
\frac{dS_V(t)}{dt} &= \gamma_m A_V(t) - \alpha\beta_m S_V(t) I_H(t)/N_H(t) - (\mu + c_m) S_V(t)\\
\frac{dE_V(t)}{dt} &= \alpha\beta_m S_V(t) I_H(t)/N_H(t) - (\mu + \theta_e + c_m) E_V(t)\\
\frac{dI_V(t)}{dt} &= \theta_e E_V(t) - (\mu + c_m) I_V(t)
\end{aligned}\right\} \quad (2)$$

with two constraints

$$N_H(t) = S_H(t) + E_H(t) + I_H(t) + R_H(t)$$

and

$$N_V(t) = A_V(t) + S_V(t) + E_V(t) + I_V(t)$$

III. LOGISTIC CURVE FITTING

Since, the Lahore dengue epidemic data is of logistic type, therefore using curve fitting method, the logistic curve can be described by the equation:

$$I_H(t) = \frac{L}{1 + \exp(\beta_0 + \beta_1 t)} \quad (3)$$

Where $I_H(t)$ is the total number of infected human at time t, L is the carrying capacity (upper limit) of the population, and β_0 and β_1 are variables that affect the shape and orientation of the logistic curve [13].

Using Lahore dengue epidemic data points from table (1) we obtained values of $\beta_0 = 1.911$ and $\beta_1 = -0.1348$. The value of carrying capacity was chosen as L = 19,220, using a combination of standard fitting techniques and visual

inspection [3]. The resulting logistic equation, fitted for the Lahore epidemic data, is

$$I_H(t) = \frac{19220}{1+\exp(1.911-0.1348t)} \quad (4)$$

TABLE I. CUMULATIVE NUMBER OF INFECTED CASES FOR DIFFERENT HOSPITAL OF LAHORE

Days	Cumulative number of infected cases
0	2476
12	3577
24	9585
40	11966
50	14981
60	17605
71	19211

IV. THE FORCE OF INFECTION AND EXPONENTIAL CURVE

"Λ" (the force of infection) is defined as a measure of the risk of a susceptible person to become infected, per unit of time t [12]. For small values of t, initially in the beginning of an epidemic, the infected number of accumulative cases can be vary as

$$I_H(t) \propto \exp(\Lambda t) \quad (5)$$

V. LOGISTIC CURVE AND EXPONENTIAL APPROXIMATION

The total number of infected human at a given time t is estimated accurately using a logistic fit and it is also approximately equal to exponential curve as shown [13]

$$I_H(t) = \frac{L}{1+\exp(\beta_0+\beta_1 t)} \propto \exp(-\beta_1 t), \text{ for small t} \quad (6)$$

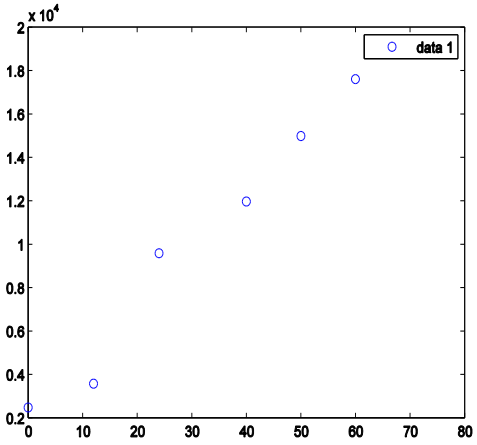

Figure 2. Cumulative number of infectious verses time (in days).

TABLE II. RELATIVE PERCENT ERROR BETWEEN LOGISTIC FIT DATA AND EXPONENTIAL APPROXIMATION

Days	Actual logistic fit	Approximation	Relative % error
1	2782.5	2833.3	1.826
2	3118.9	3242.2	3.953
3	3487.3	3710.0	6.386
4	3888.8	4245.4	9.169
5	4323.7	4858.1	12.359
6	4792.1	5559.1	16.005
7	5293.2	6361.4	20.180
8	5825.5	7279.4	24.957
9	6386.8	8329.8	30.422
10	6974.0	9531.9	36.678

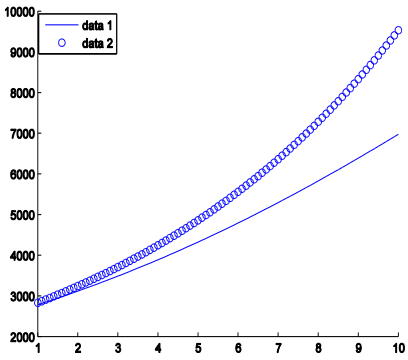

Figure 3. Data 1 shows logistic curve and data 2 shows exponentional curve

Figure (3) and Table (2) show the visual and statistical comparisons of the logistic and exponential approximations. From equation (5) and equation (6) it can be seen that $\Lambda = -\beta_1 = 0.1348$ [3].

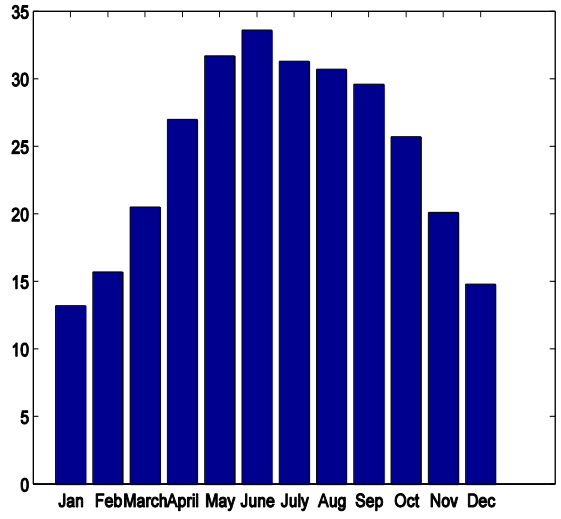

Figure 4. Monthly temperature of Lahore (Pakistan)

We collected metrological data from the metrological department of Punjab province during the epidemic year 2010-11. Data include temperature (C^0) of Lahore. The average yearly temperature of Lahore is 24.5 C^0. Graph of temperature of Lahore against months is shown in figure (4).

We also collected dengue fever data during the year 2010-11 from directorate of general health Punjab, which is used in the estimation of basic reproductive number R_0.

VI. ESTIMATION OF BASIC REPRODUCTION NUMBER R_0

The basic reproduction number R_0 is defined as "the number of secondary cases when an infected person is introduced in a totally human susceptible population".

$$R_0^2 = \left(1+\frac{\Lambda}{\mu+\theta_e+c_m}\right)\left(1+\frac{\Lambda}{\lambda+\theta_i}\right)\left(1+\frac{\Lambda}{\theta_e+c_m}\right)\left(1+\frac{\Lambda}{\lambda+\gamma}\right) \quad (7)$$

The parameters which are used in the estimation of R_0 are taken from Pinho parameter table (3). The force of infection "$\wedge$" is computed from equation (5) and equation (6). "$\wedge$" influence the basic reproduction number R_0 [2].

TABLE III. PINHO PARAMETER VALUES

Parameter	Biological name	Parameter ranges	Mean value
θ_e	Extrinsic incubation rate	0.02-0.2	0.11
θ_i	Intrinsic incubation rate	0.083-0.17	0.126
μ	Vector mortality rate	0.02-0.09	0.055
λ	Human mortality rate	0.0143-0.0167	0.015
γ	Human recovery rate	0.083-0.25	0.166
c_m	Control effort rates	0-1	0.5
δ	Average oviposition rate	0-11.2	5.6
γ_m	Average aquatic transition rate	0-0.19	0.095
k	Fraction of female mosquito hatched from all eggs	0-1	0.5
c_a or c_m	Control effort rates	0-1	0.5
α	Average bite per mosquito per day	0-1	0.5
βm	Effective contact rates	0.75	0.75

In Table (4), we estimated R_0 by using Pinho et al. 2010 [16].

TABLE IV. ESTIMATION OF R_0 FOR DENGUE EPIDEMIC (EP) DATA OF LAHORE HOSPITALS (LH) (PAKISTAN) *M* (PINHO ET AL.(2010))

EP	∧	λ	γ	μ	c_m	θ_i	θ_e	$R_{0\,(M)}$
LH data	0.13	0.02	0.17	0.06	0.5	0.13	0.11	2.2

VII. DISCUSSION AND CONCLUSION

Dengue has induced havoc impact on tropical and subtropical regions of the world. For the last few years it has badly affected the some areas of our country Pakistan especially Punjab province. This area remained under sever attack of dengue fever in 2010--2011.

In this research study, we monitored the scheme of spread of disease in Punjab province by using the proposed mathematical model of Pinho et al. (2010). In the beginning of epidemic due to correlated symptoms of dengue with flu, very few cases were registered but later on due to efficient effort of Punjab government lot of data were there in hospitals for our research study. We used some key parameters (Pinho parameters) which presents the spread of disease, other parameters are directly calculated from Punjab data e.g., β_0 = 1.911, β_1 = -0.1348 and L = 19220. Using these parameters and force of infection ($\wedge = -\beta_1$). With these values we calculated the basic reproduction number R_0. Value of R_0 describes the spread of dengue disease in Punjab. By using technique of this mathematical model one can predict the peak number of infection per day and the time at which it happened.

From our calculation of R_0, we see that dengue is epidemic in Punjab (R_0 >1) during monsoon period. Model suggests that spread of disease can be controlled by reducing the oviposition rat (δ) and exposed humans E_H (t). This can be done in very low expanses like reducing the places of stagnant water, reducing the migration of infected people I_H (t), by using mosquito's nets.

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